

Claims:

1. A method for making a porous calcium phosphate article comprising the following steps:

- i) preparing a shaped article from a paste comprising a calcium phosphate cement, a pore-forming powder and a setting liquid;
 - ii) immersing said shaped article in an immersing liquid for a first period of time so that said pore-forming powder is dissolved in the immersing liquid, creating pores in said shaped article;
 - iii) removing the resulting porous shaped article from said immersing liquid; and
 - iv) immersing the porous shaped article from step iii) in an impregnating liquid for a second period of time so that a compressive strength of the resulting article removed from the impregnating liquid is increased compared to that of said porous shaped article without said impregnating treatment,
- wherein step iii) is omitted and a compressive strength of the resulting porous shaped article removed from the immersing liquid after the first and the second periods of time is increased compared to that of the resulting porous shaped article removed after the first period of time, when the immersing liquid and the impregnating liquid are the same.

2. The method according to claim 1, wherein said pore-forming powder is selected from the group consisting of LiCl · KCl · NaCl · MgCl₂ · CaCl₂ · NaIO₃ · KI · Na₃PO₄ · K₃PO₄ · Na₂CO₃, amino acid-sodium salt, amino acid-potassium salt, glucose, polysaccharide, fatty acid-sodium salt, fatty acid-potassium salt, potassium bitartrate (KHC₄H₄O₆), potassium carbonate, potassium gluconate (KC₆H₁₁O₇), potassium-sodium tartrate (KNaC₄H₄O₆·4H₂O), potassium sulfate (K₂SO₄), sodium sulfate, and sodium lactate.

3. The method according to claim 1, wherein the immersing liquid is an acidic aqueous solution, a basic aqueous solution, a physiological solution, an organic solvent, or a substantially pure water.

4. The method according to claim 3, wherein the immersing liquid comprises at least one of Ca and P sources.

5. The method according to claim 3, wherein the immersing liquid is a
5 Hanks' solution, a HCl aqueous solution or an aqueous solution of $(\text{NH}_4)_2\text{HPO}_4$.

6. The method according to claim 3, wherein the immersing liquid and the impregnating liquid are the same.

10 7. The method according to claim 4, wherein the immersing liquid and the impregnating liquid are the same.

8. The method according to claim 5, wherein the immersing liquid and the impregnating liquid are the same.

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9. The method according to claim 1, wherein the immersing liquid and the impregnating liquid are different.

10. The method according to claim 9, wherein the impregnating liquid is
20 an acidic solution, a basic solution, a physiological solution, or a substantially pure water.

11. The method according to claim 10, wherein the impregnating liquid comprises at least one of Ca and P sources.

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12. The method according to claim 10, wherein the impregnating liquid is a Hanks' solution, a HCl aqueous solution or an aqueous solution of $(\text{NH}_4)_2\text{HPO}_4$.

30 13. The method according to claim 1, wherein the first period of time is longer than 10 minutes.

14. The method according to claim 13, wherein the first period of time is longer than 1 day.

15. The method according to claim 1, wherein the second period of time is longer than 10 minutes.

16. The method according to claim 15, wherein the second period of time is longer than 1 day.

17. The method according to claim 1, wherein the immersing in step ii) and iv) is carried out at room temperature or at a temperature between about 30 and 90°C.

18. The method according to claim 1, wherein said preparing of step i) comprises the following steps:

(a) preparing a first powder as said calcium phosphate cement comprising at least one Ca source and at least one P source, or at least one calcium phosphate source;

(b) mixing said first powder and the pore-forming powder with said setting liquid to form said paste, wherein said first powder and said setting liquid undergo a hardening reaction;

(c) molding said paste into an article in a mold of a desired shape and size before said hardening reaction is complete; and

(d) removing said molded article from said mold.

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19. The method according to claim 18, wherein said calcium phosphate source in step (a) comprises one or more calcium phosphates selected from the group consisting of alpha-tricalcium phosphate (α -TCP), beta-tricalcium phosphate (β -TCP), tetracalcium phosphate (TTCP), monocalcium phosphate monohydrate (MCPM), monocalcium phosphate anhydrous (MCPA), dicalcium phosphate dihydrate (DCPD), dicalcium phosphate anhydrous (DCPA), octacalcium phosphate (OCP), calcium dihydrogen phosphate, calcium

dihydrogen phosphate hydrate, acid calcium pyrophosphate, anhydrous calcium hydrogen phosphate, calcium hydrogen phosphate hydrate, calcium pyrophosphate, calcium triphosphate, calcium phosphate tribasic, calcium polyphosphate, calcium metaphosphate, anhydrous tricalcium phosphate,
5 tricalcium phosphate hydrate, and amorphous calcium phosphate.

20. The method according to claim 19, wherein said calcium phosphate source in step (a) is tetracalcium phosphate (TTCP).

10 21. The method according to claim 19, wherein the calcium phosphate source comprises at least one calcium phosphate particle having calcium phosphate whiskers on the surface of said calcium phosphate particle, wherein said calcium phosphate whiskers have a length of about 1-5000 nm and a width of about 1-500 nm.

15 22. The method according to claim 19, wherein the setting liquid in step (b) is an acidic solution, a basic solution, or a substantially pure water.

23. The method according to claim 22, wherein said acidic solution is
20 selected from the group consisting of nitric acid (HNO_3), hydrochloric acid (HCl), phosphoric acid (H_3PO_4), carbonic acid (H_2CO_3), sodium dihydrogen phosphate (NaH_2PO_4), sodium dihydrogen phosphate monohydrate ($\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$), sodium dihydrogen phosphate dihydrate, sodium dihydrogen phosphate dehydrate, potassium dihydrogen phosphate (KH_2PO_4), ammonium
25 dihydrogen phosphate ($\text{NH}_4\text{H}_2\text{PO}_4$), malic acid, acetic acid, lactic acid, citric acid, malonic acid, succinic acid, glutaric acid, tartaric acid, oxalic acid and their mixture.

24. The method according to claim 22, wherein said basic solution is
30 selected from the group consisting of ammonia, ammonium hydroxide, alkali metal hydroxide, alkali earth hydroxide, disodium hydrogen phosphate (Na_2HPO_4), disodium hydrogen phosphate dodecahydrate, disodium hydrogen

phosphate heptahydrate, sodium phosphate dodecahydrate ($\text{Na}_3\text{PO}_4 \cdot 12\text{H}_2\text{O}$), dipotassium hydrogen phosphate (K_2HPO_4), potassium hydrogen phosphate trihydrate ($\text{K}_2\text{HPO}_4 \cdot 3\text{H}_2\text{O}$), potassium phosphate tribasic (K_3PO_4), diammonium hydrogen phosphate ($(\text{NH}_4)_2\text{HPO}_4$), ammonium phosphate trihydrate
5 $(\text{NH}_4)_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$), sodium hydrogen carbonate (NaHCO_3), sodium carbonate Na_2CO_3 , and their mixture.

25. The method according to claim 18, wherein step (c) further comprises removing a portion of liquid from said paste, so that a liquid/powder ratio of said
10 paste decreases.

26. The method according to claim 18, wherein step (c) further comprises pressurizing said paste in said mold before said hardening reaction is complete to remove a portion of liquid from said paste, so that a liquid/powder ratio of said
15 paste decreases.

27. The method according to claim 26, wherein said pressuring is about 1 to 500 MPa.

20 28. The method according to claim 26, wherein step (c) further comprises heating said paste during said pressurizing.

29. The method according to claim 18, wherein step (c) further comprises heating said paste during molding.

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30. The method according to claim 1 further comprising removing the resulting porous shaped article having an increased compressive strength from said impregnating liquid; and cleaning and drying said porous shaped article after removed from said impregnating liquid.

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31. The method according to claim 30 further comprising heating the resulting cleaned and dried porous shaped article.

32. The method according to claim 31, wherein said heating is conducted at a temperature between 50 and 500°C.

5 33. The method according to claim 1, wherein said paste in step i) further comprises living cells.

34. The method according to claim 1, wherein said immersing liquid in step ii) comprises living cells.

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35. The method according to claim 1, wherein said impregnating liquid in step iv) comprises living cells.

36. The method according to claim 1, wherein said porous shaped article
15 having an increased compressive strength removed from said impregnating liquid in step iv) has a porosity of at least 30 vol%.

37. The method according to claim 1, wherein said porous shaped article
20 having an increased compressive strength removed from said impregnating liquid in step iv) has a porosity of 50-90 vol%.